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Systematic review

Induction of labour for suspected macrosomia at term in non-diabetic women: a systematic review and meta-analysis of randomized controlled trials

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Background Several randomized controlled trials (RCTs) compared induction of labour with expectant management in non-diabetic women with suspected fetal macrosomia.

Objective To evaluate the effects of labour induction for suspected fetal macrosomia.

Search strategy Literature search in electronic databases.

Selection criteria We included all RCTs of suspected fetal macrosomia comparing labour induction with expectant management in term pregnancy.

Data collection and analysis The primary outcome was the incidence of caesarean delivery.

Main results Four RCTs, including 1190 non-diabetic women with suspected fetal macrosomia at term, were analysed. Pooled data did not show a significant difference in incidence of caesarean delivery [relative risk (RR) 0.91, 95% confidence interval (CI) 0.76–1.09], operative and spontaneous vaginal delivery, shoulder dystocia, intracranial haemorrhage, brachial plexus palsy, Apgar score <7 at 5 min, cord blood pH <7, and mean birth weight comparing women who received induction of labour with those who were managed expectantly. The induction group had a significantly lower time to delivery (mean difference −7.55 days, 95% CI −8.20 to −6.89), lower rate of birth weight ≥4000 g (RR 0.50, 95% CI 0.42–0.59) and ≥4500 g (RR 0.21, 95% CI 0.11–0.39), and lower incidence of fetal fractures (RR 0.17, 95% CI 0.03–0.79) compared with expectant management group.

Conclusion Induction of labour ≥38 weeks for suspected fetal macrosomia is associated with a significant decrease in fetal fractures, and therefore can be considered as a reasonable option.

Keywords Caesarean, expectant management, induction, macrosomia, non-diabetic, shoulder dystocia.

Tweetable abstract #Induction of labour for #macrosomia improves neonatal outcome.

Linked article This article is commented on by ER Norwitz p. 422 in this issue. To view this mini commentary visit http://dx.doi.org/10.1111/1471-0528.14458.

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Introduction

The term macrosomia is used to describe an overweight or 'large' fetus. The common definition of macrosomia is an estimated fetal weight (EFW) of ≥4000 g, which occur in about 1–10% of all pregnancies.[1,2] Fetal macrosomia is associated with an increased risk of perinatal morbidity and mortality.[3] Intrapartum maternal and perinatal complications include prolonged labour, dystocia, operative vaginal delivery, caesarean delivery, postpartum haemorrhage, vaginal lacerations, shoulder dystocia with brachial palsy, asphyxia as well as facial nerve palsy.[3] Routine caesarean delivery for pregnancies with babies suspected to be macrosomic is not uniformly recommended. According to the American College of Obstetricians and Gynecologists (ACOG), a planned caesarean delivery may be considered

The review was registered with PROSPERO (No.: CRD42016035476).

and discussed for suspected macrosomia with a non-diabetic woman when the EFW is >5000 g, while a policy of early induction of labour in term patients with suspected fetal macrosomia was not recommended.[2] Several randomized controlled trials (RCTs) have compared induction of labour with expectant management for pregnant women with suspected fetal macrosomia.[4] However, the most appropriate management remains unclear.

The aim of this systematic review and meta-analysis of RCTs was to evaluate the effects of a policy of labour induction for suspected fetal macrosomia on mode of delivery and maternal or perinatal morbidity, compared with expectant management.

Methods

This review and meta-analysis were performed according to the recommendations in the Cochrane handbook.[5] The review protocol (PROSPERO CRD42016035476) was designed *a priori* defining methods for collecting, extracting and analysing data. The search was conducted using MEDLINE, EMBASE, Web of Sciences, Scopus, ClinicalTrial.gov, OVID and Cochrane Library as electronic databases. The citations were identified with the use of a combination of the following text words: 'macrosomia', 'labour induction', 'expectant management', 'shoulder dystocia', 'caesarean delivery' and 'randomized' from inception of each database to February 2016. Review of articles also included the abstracts of all references retrieved from the search.

Selection criteria included RCTs of induction of labour for suspected fetal macrosomia in pregnant women and/or no contraindications to planned vaginal delivery. We included only RCTs evaluating labour induction for suspected fetal macrosomia. Participants were term pregnant women with a fetus suspected to be macrosomic and without other indication of induction of labour. RCTs including only women with diabetes or gestational diabetes mellitus were excluded. Quasi-randomized trials (i.e. trials in which allocation was done on the basis of a pseudo-random sequence, e.g. odd/even hospital number or date of birth, alternation) were also excluded.

The risk of bias in each included study was assessed by using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions*.[5] Seven domains related to risk of bias were assessed in each included trial as there is evidence that these issues are associated with biased estimates of treatment effect: (1) random sequence generation; (2) allocation concealment; (3) blinding of participants and personnel; (4) blinding of outcome assessment; (5) incomplete outcome data; (6) selective reporting; and (7) other bias. Review authors' judgements were categorized as 'low risk', 'high risk' or 'unclear risk' of bias.[5]

All analyses were done using an intention-to-treat approach, evaluating women according to the treatment group to which they were randomly allocated in the original trials. The primary outcome was the incidence of caesarean delivery. Secondary outcomes were incidence of operative vaginal delivery (either forceps or vacuum), spontaneous vaginal delivery, gestational age at delivery, latency (i.e. interval from randomization to delivery), shoulder dystocia, intracranial haemorrhage, fetal fractures, brachial plexus palsy, birth weight, birth weight ≥4000 g, birth weight ≥4500 g, Apgar score <7 at 5 min, cord blood pH <7 and perinatal death. Perinatal death included fetal mortality (i.e. stillbirths) and neonatal mortality (i.e. death of a live-born baby within the first 28 days of life). Shoulder dystocia was defined as one of the following: any kind of shoulder dystocia; only significant shoulder dystocia (defined as difficulty with delivery of the shoulders that was not resolved by the McRoberts' manoeuvre); and births with an interval of 60 seconds or more between delivery of the head and the body.

Data analysis was completed using Review Manager 5.3 (Copenhagen: The Nordic Cochrane Center, Cochrane Collaboration, 2014).[5] Statistical heterogeneity between studies was assessed using the Higgins I^2 statistics. In case of significant heterogeneity ($I^2 \geq 0$), the random effects model of DerSimonian and Laird was used to obtain the pooled risk ratio estimate; otherwise, in case of no inconsistency in risk estimates ($I^2 = 0$), a fixed effect models was used.[5] The summary measures were reported as relative risk (RR) or as mean difference (MD) with 95% confidence interval (CI).

Potential publication biases were assessed graphically by using the funnel plot, and statistically by using Begg's and Egger's tests.[5] A *P*-value <0.1 was considered statistically significant.

We planned subgroup analysis for nulliparous and multiparous women for the primary outcome (caesarean delivery), as well as operative vaginal delivery.

The meta-analysis was reported following the Preferred Reporting Item for Systematic Reviews and Meta-analyses (PRISMA) statement.[6] Before data extraction, the review was registered with the PROSPERO International Prospective Register of Systematic Reviews (registration No.: CRD42016035476).

Two authors (EMM, GS) independently assessed inclusion criteria, risk of bias, data extraction and data analysis. Disagreements were resolved by discussion with a third reviewer (VB). Data from each eligible study were extracted without modification of original data onto custom-made data collection forms. Differences were reviewed, and further resolved by common review of the entire process. Data not presented in the original publications were requested from the principal investigators.

Results

Figure S1 shows the flow diagram of information derived from reviewing of potentially relevant articles. Three RCTs[7–9] and an unpublished pilot randomized trial,[10] involving 1190 women with suspected fetal macrosomia, were included in this review. All the included studies used a computer-generated table of random numbers. In three studies, sealed, sequentially numbered, opaque envelopes were used;[7,9,10] in the other trial, the method for concealment of the random allocation was not described and therefore was judged as high risk of bias.[8] All of the included studies had low risk of bias in 'incomplete outcome data'. No method of blinding as to the group allocation was reported (Figure S2). Figure S3 shows the funnel plot for the primary outcome for assessing publication bias; the symmetric plot suggests no publication bias. Publication bias, assessed using Begg's and Egger's tests, was not significant ($P = 0.75$ and 0.84, respectively).

Table 1 shows the characteristics of the included trials. All studies induced only pregnant women with singleton gestations, cephalic presentation, and suspected fetal macrosomia at term (i.e. ≥37 weeks). Women were included when ultrasound EFW, based on combination of sonographic fetal measurements, was between 4000 g and 4750 g;[7] or between 4000 and 4500 g;[8] the other two trials included women whose EFWs were above the 95th percentile at the time of inclusion.[9,10] In one trial, when EFW was ≥4500 g, scheduled caesarean delivery was performed.[8] The majority of women in the induction group were induced at ≥38 weeks. The method used for labour induction was dependent on the cervical status (prostaglandins for cervical ripening in the case of an unfavourable cervix, otherwise oxytocin infusion). The majority of women, except for one trial in which the data are not reported,[7] in the control group were expectantly managed until ≥41 weeks. Boulvain et al.[9] also enrolled women with gestational diabetes treated with diet only and excluded insulin-treated diabetes; the other three trials explicitly excluded women with diabetes or gestational diabetes mellitus[7,8,10] (Table S1).

Out of the 1190 women included in the meta-analysis, 590 (49.6%) were randomized to the induction of labour group (i.e. intervention group) and 600 (50.4%) to the expectant management group (i.e. control group). Tables 2 and 3 show the pooled data of primary, maternal and neonatal outcomes. Statistical heterogeneity within the trials was low with no inconsistency ($I^2 = 0$) in the primary outcome. Women who were randomized to induction of labour had similar incidences of caesarean delivery (26.6% versus 29.4%; RR 0.91, 95% CI 0.76–1.09; Figure 1), operative vaginal delivery (13.0% versus 15.2%; RR 0.86, 95% CI 0.65–1.13), spontaneous vaginal delivery (60.3% versus 55.4%; RR 1.09, 95% CI 0.99–1.20), shoulder dystocia (2.4% versus 4.2%; RR 0.57, 95% CI 0.30–1.08), intracranial haemorrhage (0.6% versus 0.4%; RR 1.48, 95% CI 0.20–12.57), brachial plexus palsy (0.0% versus 0.3%; RR 0.21, 95% CI 0.01–4.28), Apgar score <7 at 5 min (0.7% versus 0.5%; RR 1.51, 95% CI 0.25–9.02), cord blood pH <7 (0.2% versus 0.4%; RR 0.44, 95% CI 0.06–2.97), and had similar mean birth weight (MD −134.41 g, 95% CI −317.27 to 48.46), compared with those who did not. Women with suspected macrosomia who were randomized to induction of labour had also a significantly lower time from randomization to delivery of about 1 week (MD −7.55 days, 95% CI −8.20 to −6.89), a significantly less incidence of birth weight ≥4000 g (30.7% versus 61.8%; RR 0.50, 95% CI 0.42–0.59) and ≥4500 g (3.2% versus 14.8%; RR 0.21, 95% CI 0.11–0.39), as well as a significantly higher incidence of hyperbilirubinemia (8.8% versus 2.9%; RR 3.03, CI 1.60–5.74) and phototherapy (11.0% versus 6.6%; RR 1.68, CI 1.07–2.66) compared with expectant management group. The incidence of fetal fractures was significantly lower in the induction group compared with the control group (0.3% versus 2.0%; RR 0.17, 95% CI 0.03–0.79). Fetal fractures were reported as fractures of the clavicle or of a long bone in three studies[7,9,10] (diagnosed in two neonates in the induction group and in eight babies in the control group), and only as clavicle fracture in one study[8] (diagnosed in four neonates in the control group). No cases of perinatal death were reported. Subgroup analyses showed similar outcomes in the induction versus expectant management groups (Table S2).

Discussion

Main findings

This pooled meta-analysis of the four RCTs including 1190 women with suspected fetal macrosomia based on ultrasound EFW showed that induction of labour at term is not associated with a statistically significant difference in caesarean delivery and adverse maternal or perinatal outcomes, except for an 83% lower incidence of fetal fractures.

Strengths and limitations

Our study has several strengths. This meta-analysis included all studies published so far on the topic. The four studies collectively enrolled a large number of women. To our knowledge, no prior meta-analysis on this issue is as large, up-to-date or comprehensive. The statistical heterogeneity within the studies was low. In addition, publication bias was not apparent by statistical analysis. These are key elements that are needed to evaluate the reliability of a meta-analysis.[5]

Table 1. Characteristics of the included trials

	Tey et al. 1995[7]	Gonen et al. 1997[8]	Thornton, 1998[10]	Boulvain et al. 2015[9]
Study location	USA	Israel	UK	Multicentre**
Sample size*	40 (19 vs 21)	273 (134 vs 139)	59 (30 vs 29)	818 (407 vs 411)
Inclusion criteria	EFW between 4000 and 4750 g	EFW between 4000 and 4500 g	EFW >95th percentile	EFW ≥95th percentile***
Exclusion criteria	Any maternal or fetal indication for delivery or labour at the time of enrollment, maternal diabetes	Active labour, diabetes (either GDM or pre-gestational), previous CD, non-vertex presentation, indications for IOL other than macrosomia	Maternal diabetes except women with 2-h glucose 8–11 mmol/l, previous CD, any medical contraindication either to IOL or to allowing the pregnancy to go overdue	Any contraindication to IOL or vaginal delivery, history of CD, neonatal trauma or shoulder dystocia, severe urinary or fecal incontinence, insulin-treated diabetes
GA at induction	Between 37 and 42 weeks	≥38 weeks	Between 37^{+0} and 38^{+6} weeks	Between 37^{+0} and 38^{+6} weeks
Time to IOL after randomization	Not reported	Immediate	Within 2 days****	Within 3 days
Method of IOL	Prostaglandins E2 in Bishop score <6 followed by oxytocin	Prostaglandins or oxytocin according to the Bishop score	To the discretion of the clinician; if Bishop score <3 cervical ripening with prostaglandin or other agent	Prostaglandins E2 or misoprostol in unfavourable cervix, oxytocin if labour did not start during ripening
Expectant management	Not reported	Induction upon completion of 42 weeks	Induction by term plus 10–12 days	Induction beyond 41 weeks
GDM, diet-controlled	Excluded	Excluded	Women with 2-h glucose 8–11 mmol/l were eligible	39/407 (9.6%) vs 43/411 (10.5%)
Pre-gestational or treated GDM	Excluded	Excluded	Excluded	Excluded
Primary outcome	CD	Delivery outcome (mode of delivery, birth weight, arterial cord pH), shoulder dystocia, neonatal injury (cephalo-haematoma, clavicular fracture, brachial plexus palsy, IVH)	Maternal (CD) and fetal outcomes (brachial plexus/facial palsy, any fracture, subdural haematoma, subaponeurotic haemorrhage, hypoxic-ischaemic encephalopathy, perinatal death)	Significant shoulder dystocia, fracture of the clavicle or a long bone, brachial plexus injury, intracranial haemorrhage, death

CD, caesarean delivery; EFW, estimated fetal weight; GA, gestational age; GDM, gestational diabetes mellitus; IOL, induction of labour; IVH, intraventricular haemorrhage.
*Data are presented as total number (number in the intervention group versus number in the control group).
**France, Switzerland and Belgium.
***3500 g at 36 weeks; 3700 g at 37 weeks; 3800 g at 38 weeks.
****One case not induced as breech presentation on day of induction.

A limitation of our study was that we found only four trials that met the inclusion criteria. Two included trials, one published as an abstract and one listed as a protocol of a pilot study, had missing or unavailable data and low number of participants. We are aware that one study represents about 70% of all the women included in this meta-analysis; however, it is only by increasing the sample that we can increase the statistical power to have a more complete answer about the management of suspected fetal macrosomia at and near term.

Obstetricians may have been inclined to perform a caesarean section based on a weight >4000 g. We do acknowledge that many other outcomes, including intracranial haemorrhage, brachial plexus palsy and perinatal death, were also underpowered; however, these are indeed uncommon outcomes with an overall incidence <1% and our meta-analysis was not powered for such rare outcomes. Additionally, it is well known that ultrasound EFW, which is based on a combination of sonographic fetal measurements, is a poor predictor of fetal macrosomia.[11] Therefore, not all pregnancies included in the RCTs were carrying macrosomic neonates [birth weight ≥4000 g in 46.3% (379/818) of included pregnancies in the one trial[9] who reported this outcome]. However, mean birth weight in the expectant management group was ≥4000 g in all included studies. The inclusion of women with diet-controlled gestational diabetes in the Boulvain et al.[9] trial represents another possible limitation of our meta-analysis. However,

Table 2. Primary and maternal outcomes

	Tey et al. 1995[7]	Gonen et al. 1997[8]	Thornton, 1998[10]	Boulvain et al. 2015[9]	Total	RR or MD (95% CI)
CD	6/19 (31.6%) vs 8/21 (38.1%)	26/134 (19.4%) vs 30/139 (21.6%)	11/30 (36.7) vs 8/29 (27.6%)	114/407 (28.0%) vs 130/410 (31.7%)	157/590 (26.6%) vs 176/599 (29.4%)	0.91 (0.76–1.09)
OVD	0/19 (0.0%) vs 0/21 (0.0%)	17/134 (12.7%) vs 18/139 (12.9%)	6/30 (20.0%) vs 5/29 (17.2%)	54/407 (13.3%) vs 68/410 (16.6%)	77/590 (13.0%) vs 91/599 (15.2%)	0.86 (0.65–1.13)
SVD	13/19 (68.4%) vs 13/21 (61.9%)	91/134 (67.9%) vs 91/139 (65.5%)	13/30 (43.3%) vs 16/29 (55.2%)	239/407 (58.7%) vs 212/410 (51.7%)	356/590 (60.3%) vs 332/599 (55.4%)	1.09 (0.99–1.20)
GA at delivery	Not reported	Not reported	37.9 (37.6–38.5) vs 40.0 (39.0–41.0)	Not reported	Not reported	Not feasible
Time to delivery (days)*	Not reported	0.8 (0.08–3) vs 5.1 ± 4.0	3 (2.0–4.8) vs 18 (11–21)	4.9 ± 4.1 vs 15.4 ± 8.4	Not reported	**−7.55 days (−8.20 to −6.89)**
Perineal tear**	Not reported	Not reported	Not reported	148/407 (36.4%) vs 158/411 (38.4%)	148/407 (36.4%) vs 158/411 (38.4%)	0.94 (0.79–1.13)
Anal sphincter tear	0/19 (0.0%) vs 0/21 (0.0%)	Not reported	Not reported	6/407 (1.5%) vs 2/411 (0.5%)	6/426 (1.4%) vs 2/432 (0.5%)	3.04 (0.62–15.0)
Vaginal laceration or cervical tear	Not reported	Not reported	Not reported	5/407 (1.2%) vs 1/411 (0.2%)	5/407 (1.2%) vs 1/411 (0.2%)	5.05 (0.59–43.0)
Blood transfusion	Not reported	Not reported	Not reported	4/407 (1.0%) vs 3/411 (0.7%)	4/407 (1.0%) vs 3/411 (0.7%)	0.72 (0.30–5.98)
Haemorrhage (≥1000 ml)	Not reported	Not reported	Not reported	12/407 (2.9%) vs 21/411 (5.1%)	12/407 (2.9%) vs 21/411 (5.1%)	0.58 (0.29–1.16)
Retained placenta	Not reported	Not reported	Not reported	3/407 (0.7%) vs 4/411 (1.0%)	3/407 (0.7%) vs 4/411 (1.0%)	0.76 (0.17–3.36)
Sepsis	Not reported	Not reported	Not reported	1/407 (0.2%) vs 1/411 (0.2%)	1/407 (0.2%) vs 1/411 (0.2%)	1.01 (0.06–16.10)
Fever (38.5°C)	Not reported	Not reported	Not reported	3/407 (0.7%) vs 6/411 (1.4%)	3/407 (0.7%) vs 6/411 (1.4%)	0.50 (0.13–2.0)

CD, caesarean delivery; CI, confidence interval; GA, gestational age; MD, mean difference; OVD, operative vaginal delivery; RR, relative risk; SVD, spontaneous vaginal delivery.
Data are presented as number in the induction of labour group versus number in the control group with percentage. Boldface data, statistically significant.
*Mean ± SD or median (range).
**Episiotomy or second degree.

gestational diabetes affected only 10% of the randomized women in the study who were equally distributed in the two groups (39/407 patients in induction group and 43/411 patients in expectant management group). Gestational diabetes was treated with diet alone, and none of these pregnancies was complicated by shoulder dystocia or other neonatal complications.[12] Moreover, Thornton et al.[10] excluded women with 2-h glucose >11 mmol/l (198 mg/dl), while women with 2-h glucose 8–11 mmol/l (144–198 mg/dl) were eligible. The high number of secondary outcomes assessed by this meta-analysis could have led to a high risk of false-positive results.

Interpretation

Our meta-analysis supports earlier findings of a recent Cochrane review showing that induction of labour for suspected fetal macrosomia did not appear to alter the risk of caesarean delivery or operative vaginal delivery, but resulted in lower mean birth weight, fewer birth fractures and shoulder dystocia.[4]

In our meta-analysis, women who were randomized to induction had no statistically significant difference in the incidence of caesarean delivery (26.6%) compared with women who were managed with expectant management (29.4%). Two clinical issues deserve further comment. First, fetal macrosomia was not defined uniformly in the RCTs. The largest included RCT[9] and another one[10] used EFW >95%, while the other RCTs[7,8] used >4000 g. Probably both cutoffs could be used clinically. Second, perhaps the most difficult decision to make from these data is what gestational age should be suggested for induction. One trial,[9] which was the largest and induced women at 37^{+0}–38^{+6} weeks, was the only one that reported that the incidence of hyperbilirubinemia (≥250 mmol/l) and related phototherapy was significantly more frequent in the induction group compared with the expectant management

Table 3. Neonatal outcomes

	Tey et al. 1995[7]	Gonen et al. 1997[8]	Thornton, 1998[10]	Boulvain et al. 2015[9]	Total	RR or MD (95% CI)
Shoulder dystocia	4/19 (21.0%) vs 3/21 (14.3%)	5/134 (3.7%) vs 6/139 (4.3%)	0/30 (0.0%) vs 0/29 (0.0%)	5/407 (1.2%) vs 16/411 (3.9%)	14/590 (2.4%) vs 25/600 (4.2%)	0.57 (0.30–1.08)
Intracranial haemorrhage	0/19 (0.0%) vs 0/21 (0.0%)	3/44 (6.8%) vs 2/31 (6.4%)	Not reported	0/407 (0.0%) vs 0/411 (0.0%)	3/470 (0.6%) vs 2/463 (0.4%)	1.48 (0.20–12.57)
Fetal fracture (any)	0/19 (0.0%) vs 0/21 (0.0%)	0/134 (0.0%) vs 4/139 (2.9%)	0/30 (0.0%) vs 0/29 (0.0%)	2/407 (0.5%) vs 8/411 (1.9%)	2/590 (0.3%) vs 12/600 (2.0%)	**0.17 (0.03–0.79)**
Brachial plexus palsy	0/19 (0.0%) vs 0/21 (0.0%)	0/134 (0.0%) vs 2/139 (1.4%)	0/30 (0.0%) vs 0/29 (0.0%)	0/407 (0.0%) vs 0/411 (0.0%)	0/590 (0.0%) vs 2/600 (0.3%)	0.21 (0.01–4.28)
BW (g) Mean ± SD	4250 ± 317 vs 4253 ± 338	4062.8 ± 306.9 vs 4132.8 ± 347.4	3705 (3600–3800) vs 4000 (3800–4140)	3831 ± 324 vs 4118 ± 392	Not reported	−134.41 (−317.27 to 48.46)
BW ≥4000 g	Not reported	Not reported	Not reported	125/407 (30.7%) vs 254/411 (61.8%)	125/407 (30.7%) vs 254/411 (61.8%)	**0.50 (0.42–0.59)**
BW ≥4500 g	Not reported	Not reported	Not reported	13/407 (3.2%) vs 61/411 (14.8%)	13/407 (3.2%) vs 61/411 (14.8%)	**0.21 (0.11–0.39)**
Apgar <7 at 5 min	0/19 (0.0%) vs 0/21 (0.0%)	Not reported	Not reported	3/407 (0.7%) vs 2/411 (0.5%)	3/426 (0.7%) vs 2/432 (0.5%)	1.51 (0.25–9.02)
pH <7	Not reported	0/134 (0.0%) vs 0/139 (0.0%)	Not reported	1/407 (0.2%) vs 1/411 (0.2%)	1/541 (0.2%) vs 1/550 (0.4%)	0.44 (0.06–2.97)
Bilirubin >250 mmol/l	Not reported	Not reported	Not reported	36/407 (8.8%) vs 12/411 (2.9%)	36/407 (8.8%) vs 12/411 (2.9%)	**3.03 (1.60–5.74)**
Phototherapy	Not reported	Not reported	Not reported	45/407 (11.0%) vs 27/411 (6.6%)	45/407 (11.0%) vs 27/411 (6.6%)	**1.68 (1.07–2.66)**
Hypoglycaemia	Not reported	Not reported	Not reported	9/407 (2.2%) vs 13/411 (3.2%)	9/407 (2.2%) vs 13/411 (3.2%)	0.70 (0.30–1.62)
Admission to NICU	0/19 (0.0%) vs 0/21 (0.0%)	Not reported	Not reported	15/407 (3.7%) vs 23/411 (5.6%)	15/426 (3.5%) vs 23/432 (5.3%)	0.66 (0.35–1.25)
Transient tachypnoea	Not reported	Not reported	Not reported	1/407 (0.2%) vs 1/411 (0.2%)	1/407 (0.2%) vs 1/411 (0.2%)	1.01 (0.06–16.1)
Use of CPAP	Not reported	Not reported	Not reported	2/407 (0.5%) vs 1/411 (0.2%)	2/407 (0.5%) vs 1/411 (0.2%)	2.02 (0.18–22.2)
Perinatal death	0/19 (0.0%) vs 0/21 (0.0%)	Not reported	0/30 (0.0%) vs 0/29 (0.0%)	0/407 (0.0%) vs 0/411 (0.0%)	0/456 (0.0%) vs 0/461 (0.0%)	Not applicable

BW, birth weight; CI, confidence interval; CPAP, continuous positive airway pressure therapy; MD, mean difference; NICU, neonatal intensive care unit; RR, relative risk.
Data are presented as number in the induction of labour group versus number in the control group with percentage. Boldface data, statistically significant.

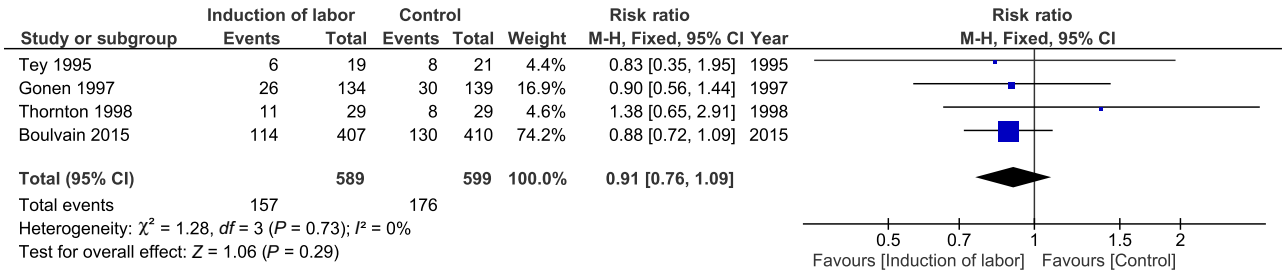

Figure 1. Forest plot for the risk of the primary outcome (i.e. incidence of caesarean delivery). CI, confidence interval; M–H, Mantel–Haenszel; df, degrees of freedom.

group. It is known that infants at $35–37^{+6}$ weeks have a significantly higher risk of severe hyperbilirubinemia (≥350 mmol/l) than those at 38–42 weeks.[13,14] The induction group in the largest trial we included[9] indeed reported that phototherapy was used especially before 38 weeks, and that none of these infants developed severe hyperbilirubinemia exceeding 350 mmol/l. Based on these data, ≥38 weeks seems like a reasonable suggestion for induction of pregnancies with suspected fetal macrosomia.

Induction of labour even in uncomplicated full-term ($39^{+0}–40^{+6}$ weeks) singleton gestations is not associated with an increased risk of caesarean delivery compared with expectant management at least until ≥41 weeks, and is associated with a significantly lower blood loss and significantly lower rate of meconium-stained amniotic fluid.[15] A systematic review and meta-analysis, including 157 randomized trials, of term and post-term labour induction reported a significant 12% decrease in the risk of caesarean delivery in singleton pregnancies.[16] This is similar to our non-significant 9% decrease in caesarean delivery. Labour induction for suspected fetal macrosomia has also been shown to be cost effective.[17]

Conclusion

We suggest ≥38 weeks induction of labour for women carrying singleton gestations with fetal macrosomia as a reasonable option. These women can be counselled that compared with expectant management until ≥41 weeks, induction is not associated with any increase in caesarean delivery or other maternal or perinatal complications, and is in fact associated with a 9% non-significant increase in vaginal delivery, an 83% significant reduction in fetal fractures, and with significantly reduced incidence of birth weight ≥4000 or ≥4500 g.

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Disclosure of interest

None declared. Completed disclosure of interests form available to view online as supporting information.

Contribution to authorship

Category 1: Conception and design of study: V. Berghella, M. Di Tommaso; acquisition of data: E.R. Magro-Malosso, M. Chen; analysis and/or interpretation of data: E.R. Magro-Malosso, G. Saccone, R. Navathe.

Category 2: Drafting the manuscript: E.R. Magro-Malosso, G. Saccone, M. Chen; revising the manuscript critically for important intellectual content: V, Berghella, M. Di Tommaso, R. Navathe.

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Details of ethics approval

Not applicable.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Figure S1. Flow diagram of studies identified in the systematic review [Prisma template (Preferred Reporting Item for Systematic Reviews and Meta-analyses)].

Figure S2. Assessment of risk of bias.

Figure S3. Funnel plot for assessing publication bias in the primary outcome (i.e. incidence of caesarean delivery).

Table S1. Characteristics of the women included in the trials.

Table S2. Cesarean delivery and operative delivery rates in subgroup analysis according to parity.■

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